UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

CASWELL FILE

DATE: March 19, 1980

SUBJECT: EPA Registration Number: 33660-11
Linuron Technical: Caswell # 528

FROM: Deloris F. Graham DFG 4/11/80
FHB/TSS E 4/18/80

TO: Bob Taylor
Product Manager (25)

Applicant: Industria Prodotti Chimici S.P.A.
(I.Pi.Ci.)
Via F. 11i Beltrami 11
Novate Milanese, Italy

Active Ingredients:

Linuron [3-(3,4-dichlorophenyl)-1-methoxy-1-methylurea].....96%
Inert Ingredients..... 4%

Background:

Acute Oral, Acute Dermal, Acute Inhalation, Eye Irritation and Skin Irritation studies were submitted in support of the conditional registration of this product. These studies were conducted at Consultox Laboratories America, Inc., Vienna, Virginia. Accession No. 232505. "Cite-All" method of support.

Recommendation:

1. The Acute Oral, Acute Dermal and Primary Dermal studies are acceptable in support of conditional registration of this product; however, for future submissions:

   a. In the Acute Oral study data must be reported in terms of individual symptomology per dose per sex, with individual necropsy reports for all animals.

   b. In the Acute Dermal study data must be reported in terms of individual symptomology per dose per sex; necropsies must be reported for all animals. Albino rabbit is the preferred test species.

   c. In the Primary Dermal Study, scores for erythema and edema at 24 and 72 hours must be reported individually for each animal.

2. The Acute Inhalation Study is core supplementary data and is not acceptable in support of conditional registration of this product.

   a. ~~There is no~~ Detailed design of chamber must be included.

   b. Must use an equal number of male and female animals.

   c. Must submit data as to actual concentration and median particle size.

   d. Must submit individual necropsy reports.

   e. Must submit body weight data.

3. The Eye Irritation Study using only 6 rabbits (Hazelton #915-104) is not acceptable in support of the conditional registration of this product.

   a. Must use 9 animals, 6 animals with unwashed eyes and 3 animals with washed eyes.

   b. Must use a dose of 0.1 ml of liquid or 100 mg of solid.

4. The Eye Irritation Study using only 3 rabbits is not acceptable in support of conditional registration of this product.

   a. Must use 9 animals, 6 animals with unwashed eyes and 3 animals with washed eyes.

   b. For solids, the correct dosage is 100 mg of formulated product.

5. FHB/TSS objects to the conditional registration of this product.

6. The appropriate toxicity category cannot be determined until an adequate Eye Irritation and Acute Inhalation study are submitted.

7. In Eye Irritation Study, Hazelton # 915-118, check spelling of product name (Liuron?).

8. On page 2 of the Eye Irritation Study (Hazelton # 915-118) under the heading "Method" check percent sodium fluorescein.

Labeling:

1. Reserve labeling comments until Eye Irritation and Acute Inhalation Studies are submitted.

2. Please refer to enclosed labeling format.

Review:

1. Acute Oral Toxicity Study: Consultox Lab. Ltd., April 1974.

Procedure: 5 M and 5 F Wistar rats (198-202g) were used at each dose level. Dose levels ranged from 1,000 mg/k to 5,000 mg/kg of Linuron Technical in 0.5% aqueous Tween 80. Observations were made for 14 days.

Results: At a dose level of 1,000 mg/kg no mortalities; at 2,000 mg/kg 2 animals died; at 3,000, 7 animals died; at 4,000, 9 animals died and at 5,000 mg/kg, all died. Symptoms observed included lethargy, disoriented locomotion, excessive salivation, chromodacryorrhea, and coma. LD_{50} was calculated to be 2600 (2122-3185) mg/kg.

Study Classification: Core Minimum Data. Response data must be reported in terms of individual symptomology per dose per sex. Individual necropsy reports must be submitted for each animal.

Toxicity Category: III - CAUTION

2. Acute Dermal Toxicity Study: Consultox Lab. Ltd., April, 1974.

Procedure: 5 M and 5 F Wistar rats (198-202 g) were administered a dose of 2000 mg/kg of Linuron Technical in 0.5% aqueous Tween 80 on abraded skin sites under occlusive wrap for 24 hours. Observations were made for 14 days.

Results: No mortalities. Symptoms observed included slight chromodacryorrhea after 24 hours. All animals asymptomatic after 72 hours. LD_{50} is greater than 2 g/kg.

Study Classification: Core Minimum Data. Response data must be reported in terms of individual symptomology per dose per sex. Used rats, preferred choice of animals is albino rabbit.

Toxicity Category: III - CAUTION

3. Acute Inhalation Study: Hazelton Lab. America, Inc. April 10, 1975; Project No. M915-103.

Procedure: 10 male rats (221-281g) were exposed to a nominal concentration of 218 mg/l of Linuron Technical for one hour. Observations were made during the treatment period and 14 day experimental period. All surviving animals were sacrificed on day 15.

Results: No mortalities. Slight hyperactivity, discharge around mouth and eyes throughout exposure period. Normal behavior observed throughout 14 day experimental observation period.

Study Classification: Core Supplementary Data.

a. Must submit detailed design of chamber.

b. Must use male and female animals.

c. Must calculate actual concentration and median particle size.

d. Must submit individual necropsy reports.

e. Must submit body weight of each animal at beginning and at each 7 day interval.

4. Eye Irritation Study: Hazelton Laboratories America, Inc. April 1, 1975. Project No. 915-104.

Procedure: 6 New Zealand white rabbits were administered a dose of 0.1 ml (148 mg) of "Liuron" into the left eye of the 3 rabbits. The treated eyes were washed 20 seconds after instillation with tap water. Observations were made at 24, 48, and 72 hours.

Results: No corneal opacity or iris irritation. Slight conjunctival redness in 3/6 at 24 hours, but had reversed itself by 48 hours.

Study Classification: Core Supplementary Data. A dose of 0.1 ml of liquid or 100 mg of solid must be used. Must use 9 animals, 6 unwashed eyes and 3 washed eyes.

5. Eye Irritation Study: Hazelton Laboratories America, Inc., April 13, 1976; Project No. 915-118.

Procedure: 3 New Zealand white rabbits were administered a dose of 0.1 ml (148 mg) of "Luiron" into the left eye of the 3 rabbits. The treated eyes were washed 20 seconds after instillation with tap water. Observations were made at 24, 48 and 72 hours.

Results: No corneal opacity or iris irritation. Slight conjunctival redness after 24 hours, but had reversed itself at 72 hours.

Study Classification: Core Supplementary Data. Must use 9 animals, 6 unwashed eyes and 3 washed eyes.

6. Dermal Irritation Study: Hazelton Lab. America, Inc., April 1, 1975; Project No. 915-105.

Procedure: 6 New Zealand white rabbits were administered a dose of 0.5 mg of Linuron Tecnical at each abraded and intact site under occlusive wrap for 24 hours. Observations were made at 24 and 72 hours.

Results: No skin irritation observed.

Study Classification: Core Minimum Data. For future submissions; scores for erythema and edema at 24 and 72 hours must be reported for each animal. Since product is a solid it should be moistened with physiological saline.

Toxicity Category: IV - CAUTION

Accession # 232505

Page 6 is not included in this copy.

Pages _____ through _____ are not included.

The material not included contains the following type of information:

____ Identity of product inert ingredients.

____ Identity of product impurities.

____ Description of the product manufacturing process.

____ Description of quality control procedures.

____ Identity of the source of product ingredients.

____ Sales or other commercial/financial information.

✓ A draft product label.

____ The product confidential statement of formula.

____ Information about a pending registration action.

____ FIFRA registration data.

____ The document is a duplicate of page(s) _____.

____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.